CLINICAL PRACTICE GUIDELINES FOR PSA TESTING AND EARLY MANAGEMENT OF TEST-DETECTED PROSTATE CANCER

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Abstract

There is a consensus among relevant peak professional bodies, government and non-government organisations in Australia, that Australian clinical practice guidelines for prostate specific antigen (PSA) testing and early management of test-detected prostate cancer are needed. Work is underway on systematic reviews of the evidence. Guideline development based on systematic review covers clinical questions relating to underlying risk of prostate cancer, PSA testing, investigation of men with positive tests and early management choices, the last relating particularly to choice among active surveillance, watchful waiting and immediate definitive treatment. National Health and Medical Research Council processes are being followed and the council's approval of the finished product will be sought. Public consultation on draft guidelines is expected to start in December 2014 and the council's approval is expected to be obtained in June 2015 or later. Planning for guideline dissemination and implementation is essential.

Over the 20 years to 2009, the number of newly-diagnosed prostate cancers in Australian men increased four-fold from 5311 in 1989 to 10,627 in 1999 and 21,808 in 2009.1 While as much as half of this was due to population ageing, age-adjusted incidence rates also increased substantially, from 92.9 per 100,000 in 1989 to 194.3 in 2009, which 2010 figures (the latest publicly available) suggest may have been the peak year.

The beginning of this doubling in rates coincided with increasing use of prostate specific antigen (PSA) testing,2 which by 2007-08 had reached annual levels of uptake in Australian men 45-74 years of age that were close to those attained by Australia’s organised screening programs for breast cancer and cervical cancer.3 Some 20% of PSA tests are done in men younger than 45 or older than 74, and research into community attitudes indicates there is widespread public confusion about the usefulness of testing.4

In late 2011, it became evident, from public statements made by the Urological Society of Australia and New Zealand, the Royal Australian College of General Practitioners, the Royal College of Pathologists of Australasia, Cancer Council Australia, Prostate Cancer Foundation of Australia (PCFA) and Cancer Australia, that there was a consensus in support of developing Australian guidelines for PSA testing for the early diagnosis of prostate cancer.5

In 2012, PCFA, in collaboration with Cancer Council Australia, undertook a consultative process that led, in November, to the first meeting of an expert advisory panel, chaired by Emeritus Professor Villis Marshall, which approved a series of clinical questions to underpin the development of Clinical Guidelines for PSA Testing and the Early Management of PSA-detected Prostate Cancer. The panel included experts in cancer control, consumer advocacy, epidemiology, general practice, medical oncology, nursing, pathology, psycho-oncology, public health, radiation oncology, rehabilitation and urology, who were nominated by the relevant Australian peak bodies. Panel members were appointed to guideline development groups for each clinical question. The need to maximise the potential benefits (reduced morbidity and mortality from prostate cancer) and minimise the potential harms of PSA-testing (resulting mainly from false positive and false negative tests and detection of prostate cancers that would not otherwise present during a man’s lifetime),6 were paramount in the panel’s thinking.

In early 2013, Cancer Council Australia’s Clinical Guidelines Network established a systematic review team, which PCFA funded, to undertake the literature reviews required to inform guideline development. These reviews use as a starting point, prior systematic reviews that underlie guidelines developed internationally with similar scope. In practice, however, few of the prior reviews have been found to have sufficient scope or to be sufficiently well done or up-to-date to facilitate the current process.
Clinical questions

The clinical questions the expert advisory panel agreed to and later refined are summarised in box 1.

**Box 1: Clinical questions for Clinical practice guidelines for PSA testing and early management of test-detected prostate cancer**

**Risk**

What risk factors can identify Australian men who are at high risk of prostate cancer or death from prostate cancer?

Suggested risk factors include:
- family history
- genotype
- ethnic origin
- obesity.

**Testing**

In men without a prior history of prostate cancer or symptoms that might indicate prostate cancer, what should be the PSA testing strategies (age to start, level at which to declare a test abnormal and frequency of subsequent testing if the PSA level is normal) for men at average risk of prostate cancer and how should they be modified, if at all, for men at high risk of prostate cancer?

What variant of PSA testing is the best to use initially?

How best can digital rectal examination (DRE) be used, if at all, in association with PSA testing?

What age or health status criteria should be used to identify men who would be unlikely to live long enough to benefit from PSA testing and who, in consequence, would not be offered PSA testing?

What methods of decision support for men about PSA testing increase men’s capacity to make an informed decision for or against testing?

What information should be given to men who are considering having a PSA test?

**Investigation**

What further tests for prostate cancer should be offered after an abnormal PSA test is obtained and before a prostate biopsy is offered?

<table>
<thead>
<tr>
<th>Candidate tests include:</th>
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<tbody>
<tr>
<td>1. repeat PSA</td>
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<tr>
<td>2. % free PSA</td>
</tr>
<tr>
<td>3. rate of increase in PSA</td>
</tr>
<tr>
<td>4. magnetic resonance imaging</td>
</tr>
<tr>
<td>5. prostate health index</td>
</tr>
<tr>
<td>6. prostate cancer antigen 3 (commonly referred to as ‘PCA3’)</td>
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<tr>
<td>7. digital rectal examination.</td>
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What constitutes an adequate prostate biopsy?

If prostate cancer is not found in an adequate biopsy, what if any additional steps should be taken and what recommendations should be made regarding the strategy for subsequent PSA testing?

What constitutes an adequate repeat prostate biopsy?

**Management**

What should be the criteria for choosing active surveillance or watchful waiting in preference to definitive treatment to offer as primary management to men who have a positive prostate biopsy?

What is the best monitoring protocol for active surveillance and what should be the criteria for intervention?

What methods of decision support for men about active surveillance increase men's capacity to make an informed decision for or against it?

What information should be given to men who are considering having active surveillance?

What is the best monitoring protocol for watchful waiting and what should be the criteria for intervention?

What methods of decision support for men about watchful waiting increase men’s capacity to make an informed decision for or against it?

What information should be given to men who are considering undergoing watchful waiting?

**Developing the guidelines**

Cancer Council Australia and PCFA are developing the guidelines in accordance with the Australian National Health and Medical Research Council’s (NHMRC’s) procedures and requirements for meeting the 2011 NHMRC standard for clinical practice guidelines outlined in box 2 (National Health and Medical Research Council. Procedures and requirements for meeting the 2011 NHMRC standard for clinical practice guidelines – Summary for developers. Melbourne: National Health and Medical Research Council; 2011.). In addition, Cancer Council Australia and PCFA will seek NHMRC approval of the guidelines, which NHMRC will give subject to compliance with a range of process requirements and conformity with the standard.
Box 2: Requirements of the NHMRC standard for clinical practice guidelines development

To meet the NHMRC standard, clinical practice guidelines must:

- provide guidance on a clearly defined clinical problem based on an identified need
- be developed by a multidisciplinary group that includes relevant experts, end users and consumers affected by the clinical practice guideline
- include a transparent process for declaration and management of potential conflicts of interest by each member of the guideline development group
- be based on the systematic identification and synthesis of the best available scientific evidence
- make clear and actionable recommendations in plain English for health professionals practising in an Australian health care setting
- be easy to navigate for end-users
- undergo a process of public consultation and independent external clinical expert review
- incorporate a plan for dissemination including issues for consideration in implementation.

We anticipate that the draft guidelines will enter the public consultation and independent external clinical expert review phases in early December 2014. Assuming they do, the earliest they can receive NHMRC approval is June 2015. Following approval, the guidelines will be published on Cancer Council Australia’s cancer guidelines wiki platform (wiki.cancer.org.au) and be made available through NHMRC’s clinical practice guidelines portal (clinicalguidelines.gov.au). It is anticipated that the wiki platform will be used to keep the guidelines up-to-date. Under present procedures, guidelines updated through the platform will not be NHMRC approved unless or until they go through the full NHMRC guideline development and approval process.

Implementation

The guidelines will do little to increase benefit or reduce harm if they are published but not used. The primary audiences for the guidelines are general practitioners advising men who are considering testing and urologists advising men who have either received a negative biopsy or who have been diagnosed with prostate cancer. While we sense relevant health practitioners are waiting for these guidelines, anticipation does not guarantee adoption in practice. Cancer Council Australia and PCFA must work with the relevant professional peak bodies, government and other non-government organisations to plan for wide dissemination and implementation as soon as the guidelines are approved.

References